

In the Specification:

Please add the following paragraph as the first paragraph of the specification:

--“This application is a National Phase application for International Application No. PCT/JP03/03944, filed March 28, 2003, which claims priority to Japanese application 2002-95590 filed March 29, 2002, the disclosures of which are incorporated herein by reference in their entireties.”--

Please amend the paragraph beginning on page 1 at line 6 as follows:

“The present invention relates to drugs and health foods including ~~anticancer agents and~~ immunopotentiators ~~for inhibiting and preventing cancer and~~ for enhancing immune system, comprising a fruit of the genus Malus such as apple (Malus domestica) and crabapple (Malus pumila), a fruit of the genus Pyrus such as a pear, or a substance derived therefrom as a raw material.”

Please amend the paragraph beginning on page 1 at line 13 as follows:

“Specifically, the present invention relates to drugs and health foods including ~~anticancer agents and~~ immunopotentiators ~~for inhibiting and preventing cancer and~~ for enhancing immune system, comprising as a raw material the above-mentioned fruit of the genus Malus, the fruit of the genus Pyrus, a substance derived therefrom as it is or as processed to juice and the like, an extract obtained by extracting the above-mentioned fruit of the genus Malus or the fruit of the genus Pyrus with water or an organic solvent such as alcohol, or a substance derived from the extract. The present invention further relates to drugs and health foods including ~~anticancer agents and~~ immunopotentiators ~~for inhibiting and preventing cancer and~~ for enhancing immune system, comprising a mature fruit and/or an immature fruit of the genus Malus such as apple (Malus domestica) and a crabapple (Malus pumila), or a fruit of the genus Pyrus as a raw material.”

Please amend the paragraph beginning on page 2 at line 6 as follows:

“Conventionally, it has been known that an extract of Cordyceps sinensis, when administered as a drug such as ~~an anticancer agent or an~~ immunopotentiator and a health food, has the effects of enhancing the innate immune system such as natural killer cells, macrophages

and the like, in addition to suppressing the growth of existing cancer cells, and when taken regularly, it further has the effect of preventing the onset of cancer, that is, the cancer preventing effect (for example, see Patent Document 1)."

Please amend the paragraph beginning on page 4 at line 4 as follows:

"However, medical or pharmaceutical studies on the pharmacological effects of the apple have been rarely carried out, but the similar studies on health food containing apple vinegar as a supplementary ingredient ~~and immune-system-strengthening food containing apple (Malus domestica)~~ have been proposed. However, studies on the ~~anticancer action or the~~ immunopotentiating action of the apple fruit have not been conducted, ~~except for the research by Miura et al., School of Medicine at Hirosaki University, which reports the finding that apple polyphenol has an antitumor effect.~~"

Please amend the paragraph beginning on page 4 at line 15 as follows:

"In other words, a specific study related to the pharmacological effects of apple itself has not been carried out, and the mechanism of the pharmacological effects has not yet been clarified, and further studies on apple as ~~an anticancer agent~~, an immunopotentiator, or a cancer-preventing agent have not been tried at all."

Please amend the paragraph beginning on page 5 at line 11 as follows:

"An object of the invention described in claims 1 to 3 and 6 in the present inventions is to enhance the innate immune system such as natural killer cell[[s]], a macrophage[[s]] ~~and or the~~ like, or the activity of lymphocyte[[s]], and thus ~~prevent or suppress cancer in addition to inhibiting the growth of cancer cells~~ obtain a higher immunopotentiating effect by using both a mature fruit and an immature fruit of a fruit of the genus Malus such as apple (Malus domestica) and crabapple (Malus pumila), or a fruit of the genus Pyrus."

Please delete the paragraph beginning on page 5 at line 23 and ending on page 6 at line 1,

Please amend the paragraph beginning on page 6 at line 3 as follows:

"The present inventors have found that a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), a fruit of the genus *Pyrus*, or a substance derived therefrom, ~~has an anticancer effect or a cancer suppressing effect~~ has the higher immunopotentiating effect by initially carrying out various animal tests, and then on humans, to thus complete the present inventions."

Please amend the paragraph beginning on page 6 at line 10 as follows:

"To achieve the above-mentioned objects, the invention described in claim 1 in the present inventions is directed to a drug such as ~~an anticancer agent or an immunopotentiator~~, which is characterized by comprising both a mature fruit and an immature fruit of a fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), a fruit of the genus *Pyrus*, or a substance derived therefrom as an active ingredient."

Please amend the paragraph beginning on page 6 at line 17 as follows:

"The invention described in claim 2 is characterized by the constitution of using an aqueous extract of both the mature fruit and the immature fruit of the fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), the fruit of the genus *Pyrus*, or a substance derived from the aqueous extract, in addition to the constitution of the invention described in claim 1."

Please amend the paragraph beginning on page 6 at line 22 as follows:

"The invention described in claim 3 is characterized by the constitution of using an extract of both the mature fruit and the immature fruit of the fruit of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), the fruit of the genus *Pyrus* obtained by extraction with an organic solvent such as alcohol, or a substance derived from the extract, in addition to the constitution of the invention described in claim 1."

Please amend the paragraph beginning on page 7 at line 8 as follows:

"It has been revealed that the effects of invention described in claims 1 to 3 obtained from such constitutions, consist in that both the mature fruit and the immature fruit of a fruit of

the genus Malus such as apple (Malus domestica) and crabapple (Malus pumila), a fruit of the genus Pyrus, a substance therefrom, an extract obtained by extracting the fruit with water or an organic solvent such as alcohol, or a substance derived from the extract, when administered, enhances the immune system such as natural killer cells, macrophages and the like to control cancer-attacked cells, as well as to prevent carcinogenesis of cells not yet attacked by cancer, and when taken regularly, has the effect of preventing the onset of cancer obtain higher immunopotentiating effect and thus has the effect of preventing the onset of cancer, that is, the cancer preventing effect.”

Please amend the paragraph beginning on page 7 at line 21 as follows:

“The invention described in claim 4 is characterized by the constitution of administering as a raw material an extract of both the mature fruit and the immature fruit of the fruit of the genus Malus such as apple (Malus domestica) and crabapple (Malus pumila), the fruit of the genus Pyrus, or a substance derived from the extract orally, percutaneously, parenterally, or via other routes, in addition to the constitution of the invention described in claim 1, 2, or 3.”

Please delete the paragraph beginning on page 8 at line 10 and ending on page 8 at line 16.

Please delete the paragraph beginning on page 8 at line 17 and ending on page 8 at line 22.

Please amend the paragraph beginning on page 8 at line 23 as follows:

“The invention described in claim 6 is a health food ~~for inhibiting and preventing cancer~~ ~~or~~ for enhancing immune system, comprising the mature fruit and the immature fruit of a fruit of the genus Malus such as apple (Malus domestica) and crabapple (Malus pumila), a fruit of the genus Pyrus, or a substance derived therefrom as a raw material.”

Please delete the paragraph beginning on page 9 at line 15 and ending at line 20.

Please delete the paragraph beginning on page 9 at line 21 and ending on page 10 at line

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Please amend the paragraph beginning on page 26 at line 23 as follows:

In addition, the antitumor effect and the immunopotentiating effect of crabapple (*Malus pumila*) or a fruit of the genus *Pyrus* which has more polyphenol per unit weight, as compared to apple *Malus domestica*, were investigated in the same manner as in the above-described test. The fruit was made into a juice with the fruit skin included and the fruit core removed by a juicer and taken by mice. Further, the antitumor effect was investigated when crabapple (*Malus domestica-pumila*) was made into a juice by a juicer with the fruit skin included, and mixed with a juice of a mature fruit of the genus *Malus domestica*. This was carried out for the purpose of developing a functional food or a drug which elevates the antitumor effect and the immunopotentiating effect by enhancing the frequencies of pectin and polyphenol by mixing the pectin which is contained in a large amount in the juice of a mature fruit of the genus *Malus domestica*, with the polyphenol which is contained in a large amount in a fruit of the genus *Malus pumila* (crabapple) or a fruit of the genus *Pyrus*."

Please amend the paragraph beginning on page 27 at line 17 as follows:

"As the results of the test for the mice, it has been observed that a juice of a mature fruit of the genus *Malus domestica* which is mixed with a juice of an immature fruit thereof, a fruit juice of crabapple (*Malus domestica-pumila*), or with the genus *Pyrus*, when administered, has a higher antitumor effect or immunopotentiating effect, as compared to a juice of a mature fruit of the genus *Malus domestica* alone. Further, it has been proven that such mechanism activates the "innate immune system" such as natural killer cells, macrophages and the like, as well as increases the frequency and the function of killer T-cells or helper T-cells"

Please delete the paragraph on page 30 at line 25.

Please amend the paragraph beginning on page 31 at line 1 as follows:

As described above, it has been observed that the invention described in claims 1 to 3 or 6 in the present inventions has the effects that both a mature fruit and an immature fruit of a fruit

of the genus *Malus* such as apple (*Malus domestica*) and crabapple (*Malus pumila*), a fruit of the genus *Pyrus*, a substance derived therefrom, an extract by extracting the fruit with water or an organic solvent such as alcohol, or a substance derived from the extract, when administered, enhances the innate immune system such as natural killer cells, macrophages and the like to control cancer-attacked cells, as well as to prevent carcinogenesis of cells not yet attacked by cancer, and when taken regularly, has the effect of preventing the onset of cancer, that is, the cancer preventing effect.”

Please amend the paragraph beginning on page 32 at line 15 as follows:

“It has been proven that ~~the invention described in claims 5 and 7~~ has the effect that a mixture of a mature fruit of the genus *Malus domestica* (apple) with an immature fruit thereof or a fruit of crabapple (~~*Malus domestica pumila*~~) has a ~~higher antitumor effect or a higher~~ immunopotentiating effect, as compared to a mature fruit of the genus *Malus domestica* alone, in addition to the effects of the invention described in claims 1 to 4 or 6.”